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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,003	11/06/2001	Richard Allen Rosenbloom	QUIG-1006US	5759

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EXAMINER	
HUI, SAN MING R	
ART UNIT	PAPER NUMBER
1617	6

DATE MAILED: 11/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,003	ROSENBLOOM, RICHARD ALLEN	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendments filed June 24, 2002 have been entered.

The outstanding rejections under 35 USC 112, second paragraph are withdrawn in view of the amendments filed June 24, 2002.

Information Disclosure Statement

Applicants' IDS submitted February 21, 2002 in Paper No. 3 is acknowledged. Some non-patent literature documents, e.g., articles downloaded fromt he internet, have been crossed out as they are not appropriate for IDS, i.e., no name of author and no publicaitno data (e.g., date and page) provided.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 16-20 of

copending Application No. 10/132,642 and 10/045,790. Although the conflicting claims are not identical, they are not patentably distinct from each other because the differences between the instant application and the copending application is that the instant application are drawn to the method of preventing, treating or reducing radiation dermatitis caused by specific ionized radiation such as alpha radiation, beta radiation, gamma ray radiation, and x-ray radiation. One of ordinary skill in the art would reasonably expected to employ the same composition containing the same class of compound to treat or reduce radiation dermatitis broadly, because the instant composition is effective to treat or reduce radiation dermatitis caused by specific radiation.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, and 6-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some specific vitamin D compounds disclosed in the instant specification page 3-6, does not reasonably provide enablement for other compounds that inhibit at least one of cell differentiation and cell proliferation. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that define "compounds that inhibits at least one of cell differentiation and cell proliferation". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "compounds that inhibits at least one of cell differentiation and cell proliferation" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art

is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on all "compounds that inhibits at least one of cell differentiation and cell proliferation", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claim 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant claims are drawn to the prevention of radiation dermatitis. The specification discloses the vitamin D compounds being useful as cell proliferation inhibitors. However, the specification fails to adequately teach how to use the method to prevent radiation dermatitis. Radiation dermatitis is the damage of the skin that is resulted from high-energy exposure. There is only one method to prevent radiation dermatitis known, which is the complete blockage of the radiation (See Chapman from the Medscape Dermatology Clinic). Thus, it is clear from the teachings of Capman that the ability to prevent radiation dermatitis caused by high-energy radiation is highly unlikely and unpredictable and has met with very little success. For chronic radiation dermatitis, no treatment is even needed, according to Chapman. Applicants have not provided any convincing evidence that their claimed invention is indeed useful as preventive for radiation dermatitis caused by high-energy radiation and have not provided sufficient guidance to allow one skilled in the art to practice the

claimed invention without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are drawn to a method for the prevention, reduction or treatment of radiation dermatitis caused by one or more types of radiation selected from the group consisting of alpha radiation, beta radiation, gamma ray radiation and x-ray radiation". The inclusion of the specific types of radiation is not disclosed in the instant specification. Applicant is required to cancel such limitations.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "compounds that inhibits at least one of cell differentiation and cell proliferation" in claim 1 renders the claims indefinite as to compounds encompassed thereby. Please note that only certain numbers of vitamin D compounds are disclosed

in the instant specification. It is not clear what other compounds, other than the ones disclosed in the specification, page 3-6, are encompassed by the claims herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kita (WO97/18817, English equivalent US Patent 6,162,801), Darr et al. (British Journal of Dermatology, 1992; 127:247-253 from IDS received February 21, 2002), and Sine et al. (US Patent 5,972,359). All the references, except Darr et al., are references of record in the previous office action mailed January 15, 2002)

Kita teaches a vitamin D3 composition useful as skin treatment for protecting skin against the effects and damage of ultraviolet radiation (See col. 9, lines 43-48, column

10, lines 50-54). Kita also teaches the effective dosage of vitamin D3 as 0.01-100μg/ml (See col. 9, line, 8-10).

Darr et al. teaches that vitamin C or vitamin E, when administered orally or topically, is useful as treatment for ultraviolet radiation-induced damage (See Summary and page 247).

Sine et al. teaches a method of treating skin to reduce the effects of ultraviolet radiation exposure, comprising applying a composition that comprises the antioxidants, such as tocopherol acetate (vitamin E) and retinal (vitamin A), and D-panthenol, in a pharmaceutical acceptable carrier comprising acrylic copolymers, Carbopol® 954 and Carbopol® 1382 (which are known copolymers of acrylic acid and a polyallyl sucrose) which are dissolved in polyethylene glycol (See col. 3, lines 30-35, col. 39, especially Phase C: items 3 and 4, Phase D: items 4 and 9, Phase F: item 1, Phase H: item 3, lines 35-67).

The references do not expressly teach the method of treating radiation dermatitis caused by ionized radiation employing vitamin D3 and the antioxidants, and the excipients together. The references do not expressly teach the amount of the compounds employed.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ vitamin D3 and the antioxidants, and the excipients together in a method of treating radiation dermatitis caused by ionized radiation. It would have been obvious to one of ordinary skill in the art at the time the invention was

made to employ the herein claimed amount of the compounds in the method of treating radiation dermatitis caused by ionized radiation.

One of ordinary skill in the art would have been motivated to employ vitamin D3 and the antioxidants, and the excipients together in a method of treating radiation dermatitis caused by ionized radiation. The active ingredients herein, i.e., vitamin D3, the herein claimed antioxidants (vitamin A and E), and D-panthenol, are known to be useful to treat UV radiation damage individually. Combining these agents into a single composition useful for the same purpose is obvious (See *In re Kerkhoven* 205 USPQ 1069). The difference between UV radiation and the herein claimed radiation is that the herein claimed radiation has higher energy and therefore the damage afflicted by such radiation is considered as more intense and severe. Possessing the teachings of the cited prior art, one of ordinary skill in the art would be reasonably expect to treat the radiation dermatitis caused by radiation caused by either low energy radiation or high energy radiation, such as the herein claimed radiation, using the combination of the herein claimed actives since the different in the radiation induced damage being considered as different in degree, not different in kind. Therefore, absent evidence to the contrary, if the herein claimed compounds are useful to treat less intense damage caused by low energy radiation, one would have been reasonably expected to employ the same composition, which contains the herein claimed compounds, to treat or ameliorate symptoms of the more severe and intense damage.

One of ordinary skill in the art would have been motivated to employ the herein claimed amount of the active compounds in the method of treating radiation dermatitis

caused by ionized radiation since the optimization of the result effect parameters (e.g., amounts of the actives and excipients) is obvious as being within the skill of the artisan.

Claims 1, 9, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kita (WO97/18817, English equivalent US Patent 6,162,801), Darr et al. (British Journal of Dermatology, 1992; 127:247-253), and Sine et al. (US Patent 5,972,359) in view of Neigut (US Patent 6,048,886), Schonrock et al. (US Patent 5,876,737) and Gers-Barlag et al. (US Patent 5,952,391), references of record.

Kita, Darr et al., and Sine et al. suggest the method of treating radiation dermatitis caused by herein claimed ionized radiation employing the herein claimed compounds, in the herein claimed amount (see above).

The references do not expressly teach the employment of α-lipoic acid, or hydroxymethylcellulose, or one or more antioxidant enzymes, in the method for treating radiation dermatitis therein. The references do not expressly teach the herein claimed amount of the actives and excipients for the method of treating the same.

Neigut et al. teaches a composition comprising vitamin A, D, and E, α-lipoic acid, and an antioxidant enzyme, superoxide dismutasem in a corn oil vehicle for the topically treating UV radiation damage, such as dermatitis (See col. 1, lines 42-46; col. 4, lines 38-60; col. 5, lines 29-35; col. 7, Compound II, lines 40-60; col. 11, line 59 – col.13, line 60).

Schonrock et al. teaches a composition of α-tocopherol acetate and hydroxypropylmethylcellulose or hydroxymethylcellulose, useful for sunscreen and

treating UV radiation induced damage (See col. 1, line 66 – col. 2, line 5, 39-44; col. 14, lines 1-44).

Gers-Barlag et al. teaches the quercetin, when topically administered, is useful in a method of treating UV radiation induced damage (See col. 1, line 6 trough col. 2, line 38; col. 14, line 25 through col. 15, line 20).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the references by combining the method suggested by Kita, Darr et al., and Sine et al. (see above) of treating radiation dermatitis employing vitamin D3, vitamin E acetate, and vitamin A by also employing α-lipoic acid and/or hydroxymethylcellulose as a carrier, and/or one or more antioxidant enzymes, such as superoxide dismutase, and/or quercetin, and/or corn oil base carrier in the amounts recited herein in a topical composition in the same method of treating ionized radiation induced radiation dermatitis.

One of ordinary skill in the art would have been motivated to incorporate at least one more antioxidant and/or antioxidant enzymes, such as superoxide dismutase, with α-lipoic aicd and/or quercetin into the radiation dermatitis treating composition suggested by Kita, Darr et al., and Sine et al., and employ such composition to treat ionized radiation induced radiation dermatitis. Vitamin E, superoxide dismutase, α-lipoic acid, and quercetin are known to be useful for treating radiation dermatitis. Combining these agents together useful for the same purpose is obvious (See *In re Kerkhoven* 205 USPQ 1069). Employing such UV radiation dermatitis treating composition for treating radiation dermatitis caused by herein claimed ionized radiation dermatitis would also be

obvious to one of ordinary skill in the art, absent evidence to the contrary (See above). Furthermore, The optimization of result effect parameters (e.g., amounts of the actives and excipients) is obvious as being within the skill of the artisan.

Response to Arguments

Applicant's arguments with respect to claims 1-11 have been considered but are moot in view of the new ground(s) of rejection.

obvious to one of ordinary skill in the art, absent evidence to the contrary (See above). Furthermore, The optimization of result effect parameters (e.g., amounts of the actives and excipients) is obvious as being within the skill of the artisan.

Response to Arguments

Applicant's arguments with respect to claims 1-11 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
November 7, 2002

SREENI PADMANABHAN
PRIMARY EXAMINER

11/16/02